UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/103,355 | 06/23/1998 | PETER J. KUSHNER | 2307O-080510 | 2899 |

22798 7590 06/16/2006

QUINE INTELLECTUAL PROPERTY LAW GROUP, P.C.
P O BOX 458
ALAMEDA, CA 94501

| EXAMINER | |
|---|---|
| PAK, MICHAEL D | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1646 | |

DATE MAILED: 06/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/103,355 | KUSHNER ET AL. | |
| | Examiner | Art Unit | |
| | Michael Pak | 1646 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *30 December 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-13 and 16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13, 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Response to Amendment*

1. Amendment filed December 30, 2005 has been entered.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Applicant's arguments filed December 30, 2005, have been fully considered but they are not found persuasive.

### *Claim Rejections - 35 USC § 103*

4. Claims 1-13 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kushner et al.((AB); U.S. 5,723,291) in view of Pfahl et al.((A); U.S. 6,004,748), Evans et al.((B); U.S. 5,639,592), GAUB et al.((AV); Cell, 1990), Webb et al.(CB) and Kushner et al.((AD); WO 95/06754).

Kushner et al. teach a method with a cell or cells which express the estrogen receptors, Fos, jun, and AP-1 promoter fused to CAT gene (columns 4-8, 10-12, and 17-20). The cells were contacted with estrogen which resulted in detection of the reporter CAT (column 10). Furthermore, Kushner et al. teach a method using MDA453 cells (columns 5, 14 and 15) which express endogenous estrogen receptor by transfecting with estrogen receptor fusion protein (columns 13-15). The assays are performed with and without hormones (columns 13-15). Both fos and jun are in the

methods of the assays in order for the AP-1 sites to work and thus are in contact with the cells. The cells are co-transfected with both estrogen receptor and Jun/Fos (column 13). The jun in the cell is c-jun (column 10). There are more than one cell in the assay. The negative control is taught by transfection with or without jun or fos at the same time or singly (columns 10 and 13). The estrogen receptor fusion protein or modified receptor is used in the transfected cells (column 6). Kushner et al. does not teach a cognate receptor which is not estrogen receptor.

Evans et al. teach the method using a cell (such as HeLa, CV-1, NIH-3T3 cells; column 8) comprising c-jun, fos (column 5), and nuclear receptors (such as glucocorticoid, retinoic acid, estrogen, androgen, progesterone, vitamin D3, mineralcorticoid receptors; columns 6, 8-16). The column 7 teaches the method using AP-1 proteins by exogenous expression. Furthermore, column 5 teaches the method using AP-1 proteins endogenously or by administering fos or jun. Column 6 teaches the method using the estrogen receptor. The pages 7-8 of the specification's definition of "AP-1 mediated estrogen activity" is generic to the teachings of Evans et al. and does not exclude the teachings of Evans et al. Kushner provide evidence that HeLa, CV-1, and NIH-3T3 cells inherently express estrogen receptor (column 12, Table I). The phorbol ester interaction activates the AP-1 which can be the transcription factor ligand for the protein kinase C which is the "cognate receptor" which is not excluded by the definitation in the specification on page 6, lines 13-14.

Pfahl et al. teaches a method of detecting AP-1 interaction with cell containing estrogen receptors and as well as AP-1 promoter (columns 1-3 and 7-8). Columns 2

and 4 teaches the method using AP-1 proteins, cJun and cFos, by exogenous expression. Furthermore, column 2 teaches the method using AP-1 proteins endogenously expressing fos or jun. Column 2 teaches the method using the estrogen receptor. The pages 7-8 of the specification's definition of "AP-1 mediated estrogen activity" is generic to the teachings of Pfahl et al. and does not exclude the teachings of Pfahl et al. including effects of dexamethasone. Kushner provide evidence that HeLa, CV-1, and NIH-3T3 cells inherently express estrogen receptor (column 12, Table I).

GAUB et al. teach a method using the cell comprising estrogen receptor, ovalbumin element which is target for transactivation by c-fos and c-jun linked to CAT reporter(page 1271 and figure 6). Cells are contacted with TPA or forskolin and the receptor(HE0) and fos and jun and reporter activity measured (page 1271 and figure 6). Page 6, lines 1-2, defines nuclear transcription ligand as a compound that binds to a nuclear transcription factor thus both fos and jun are nuclear receptors and ligands because they are transcription factors and they bind to each other. TPA and forskolin activates the cell thus are compounds which have AP-1 mediated estrogenic activity. A second cell and figure 6 were performed with more than one cell in a cell culture which comprises the all the elements of the first cell . Limitation that the cells are the same which is met above. Claims 4 and 5 definition of "cognate receptor" in the specification on page 6, lines 13-14, does not further limit claim than the receptor in claims 2 and 3.

Webb et al.(CB) and Kushner et al.((AD); WO 95/06754) are cumulative reference with Kushner et al.((AB); U.S. 5,723,291) Pfahl et al.((A); U.S. 6,004,748), Evans et al.((B); U.S. 5,639,592), and GAUB et al.((AV); Cell, 1990).

It would have been obvious to modify the method of Kushner et al.((AB); U.S. 5,723,291) by incorporating the teaching of Pfahl et al.((A); U.S. 6,004,748), Evans et al.((B); U.S. 5,639,592), and GAUB et al.((AV); Cell, 1990) and further use the glucocorticoid receptor, retinoic acid receptor, or other nuclear receptors as cognate receptors which are not estrogen receptor. One of skilled in the art would have been motivated combine the teaching of the references because they are analogous references which teach nuclear receptors interaction with AP-1 site and AP-1 protein interaction. Further motivation is provided by Evans et al. who teach that understanding the mechanism of the regulatory effect of hormones, receptors, and AP-1 transcription factors are important to determine undesirable side effects especially as it relates to proto-oncogenic effects of cell growth and differentiation (columns 1 and 2). Evans et al. motivation is especially important in view of the regulatory interaction of estrogen signalling pathway with glucocorticoid, progestins, and androgens as taught by Gaub et al. (Pages 1267 and 1273). Further motivation is provided by Pfahl et al. who teach that methods of the invention can be used to identify and screen new ligand of nuclear receptor useful for treatment of cancer because the receptors (such as estrogen and glucocorticoid etc.) interaction with AP-1 (columns 1-3).

Applicants argue that none of the references discuss the additional limitation of a cell contating an estrogen receptor and a cognate receptor for a transcription factor ligand that is not necessarily present in the cell. However, the combination of the references provide the cognate receptor for a transcription factor ligand which is not estrogen receptor.

Applicants argue that the cited references do not teach all the limitations of the claim. However, Kushner et al. teaches all the limitations except the additional cognate receptor which is not estrogen receptor. The additional references provide cognate receptors that are not estrogen receptor i.e. glucocorticoid receptor, retinoic acid receptor and other nuclear receptors.

Applicants argue that Evans do not provide the motivation because the reference does not direct one the screening of the ligands. However, the motivation provided was to directed to the screening of the ligands. Furthermore, the references are analogous providing easily available substitution of material to improve the method steps.

Applicants argue that the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified. However, the nature of progress in science is improvement upon previous inventions and the references are analogous art whose references are well known to one of ordinary skill in the art to use as motivation to add method steps.

Applicants argue that presence of chemicals such as phorbal esters found in many of the cited references would create reporter signal noise rendering modulation by cognate receptors undiscernable or incaplabe of interpretation in the screening methods. However, applicants provides no evidence that such problems exist. Furthermore, phorbal ester is just on of the screening compounds used. Applicants argue that there is no expectation of success. However, the state of the art is cumulative and analogous art and is well known to one of ordinary skill in the art.

***Double Patenting***

5. Claims 1-13 and 16 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-27 of U.S. Patent No. 5,723,291 in view of Pfahl et al.((A); U.S. 6,004,748), Evans et al.((B); U.S. 5,639,592), GAUB et al.((AV); Cell, 1990), Webb et al.(CB) and Kushner et al.((AD); WO 95/06754). Although the conflicting claims are not identical, they are not patentably distinct from each other.

The reason for the rejection has been set forth in the previous office action.

The teachings of Pfahl et al.((A); U.S. 6,004,748), Evans et al.((B); U.S. 5,639,592), GAUB et al.((AV); Cell, 1990), Webb et al.(CB) and Kushner et al.((AD); WO 95/06754) are discussed above.

Cognate receptors which are not estrogen receptor are not taught by Kushner et al.((AB); U.S. 5,723,291).

It would have been obvious at the time of the invention to modify the method of claims 1-27 of U.S. Patent No. 5,723,291 by incorporating the teaching of Pfahl et al.((A); U.S. 6,004,748), Evans et al.((B); U.S. 5,639,592), and GAUB et al.((AV); Cell, 1990) and further use the glucocorticoid receptor, retinoic acid receptor, or other nuclear receptors. One of skilled in the art would have been motivated combine the teaching of the references because they are analogous references which teach nuclear receptors interaction with AP-1 site and AP-1 protein interaction with interests in understanding cancer cell growth regulation. Further motivation is provided by Evans et al. who teach that understanding the mechanism of the regulatory effect of hormones, receptors, and

AP-1 transcription factors are important to determine undesirable side effects especially as it relates to proto-oncogenic effects of cell growth and differentiation (columns 1 and 2). Evans et al. motivation is especially important in view of the regulatory interaction of estrogen signalling pathway with glucocorticoid, progestins, and androgens as taught by Gaub et al. (Pages 1267 and 1273). Further motivation is provided by Pfahl et al. Wwho teach that methods of the invention can be used to identify and screen new ligand of nuclear receptor useful for treatment of cancer because the receptors (such as estrogen and glucocorticoid etc.) interaction with AP-1 (columns 1-3).

6. No claims are allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Pak whose telephone number is 571-272-0879. The examiner can normally be reached on 8:00 - 2:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on 571-272-0835. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9306 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Michael D. Pak

Michael Pak
Primary Examiner
Art Unit 1646
7 June 2005